

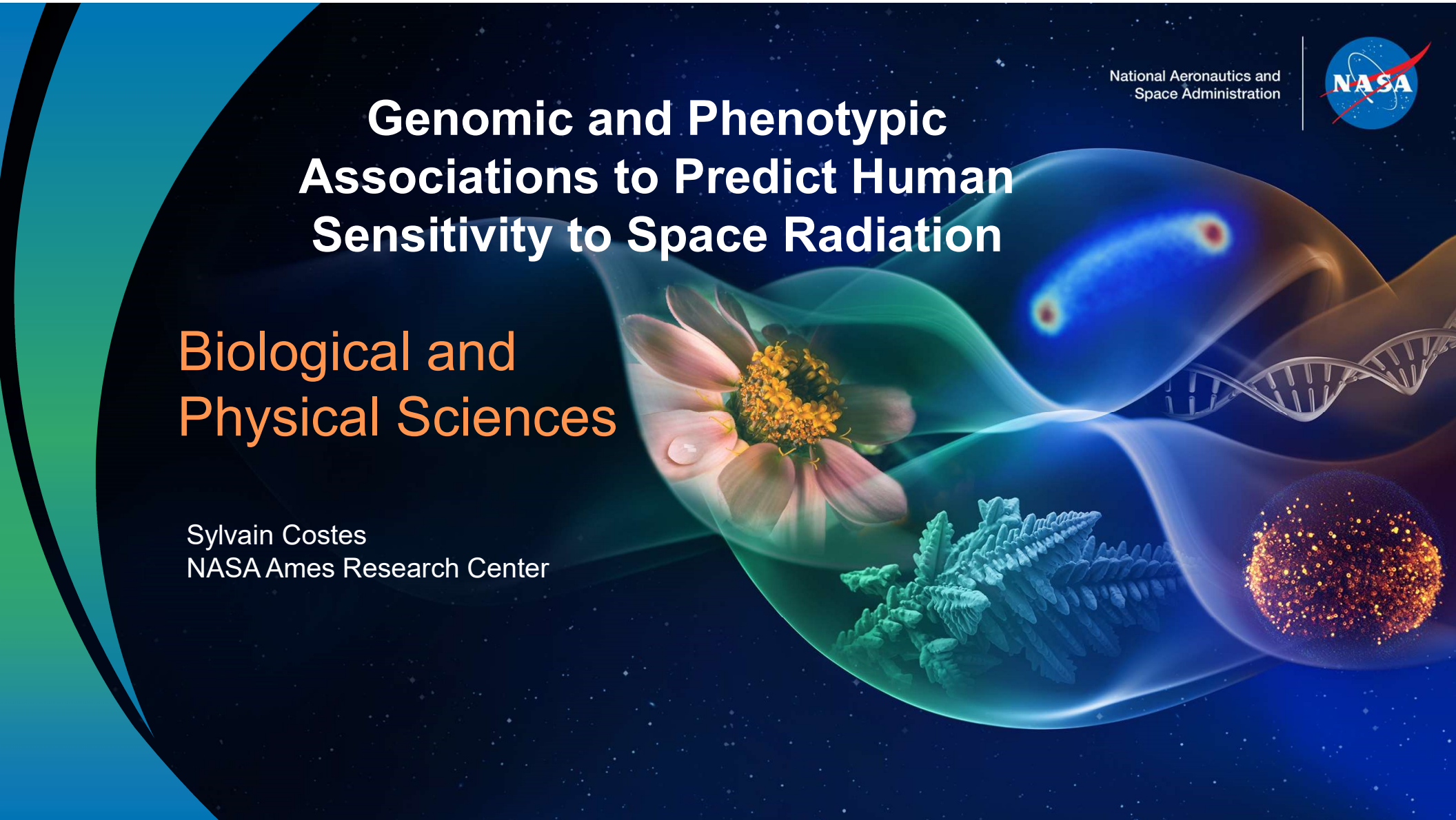
National Aeronautics and
Space Administration



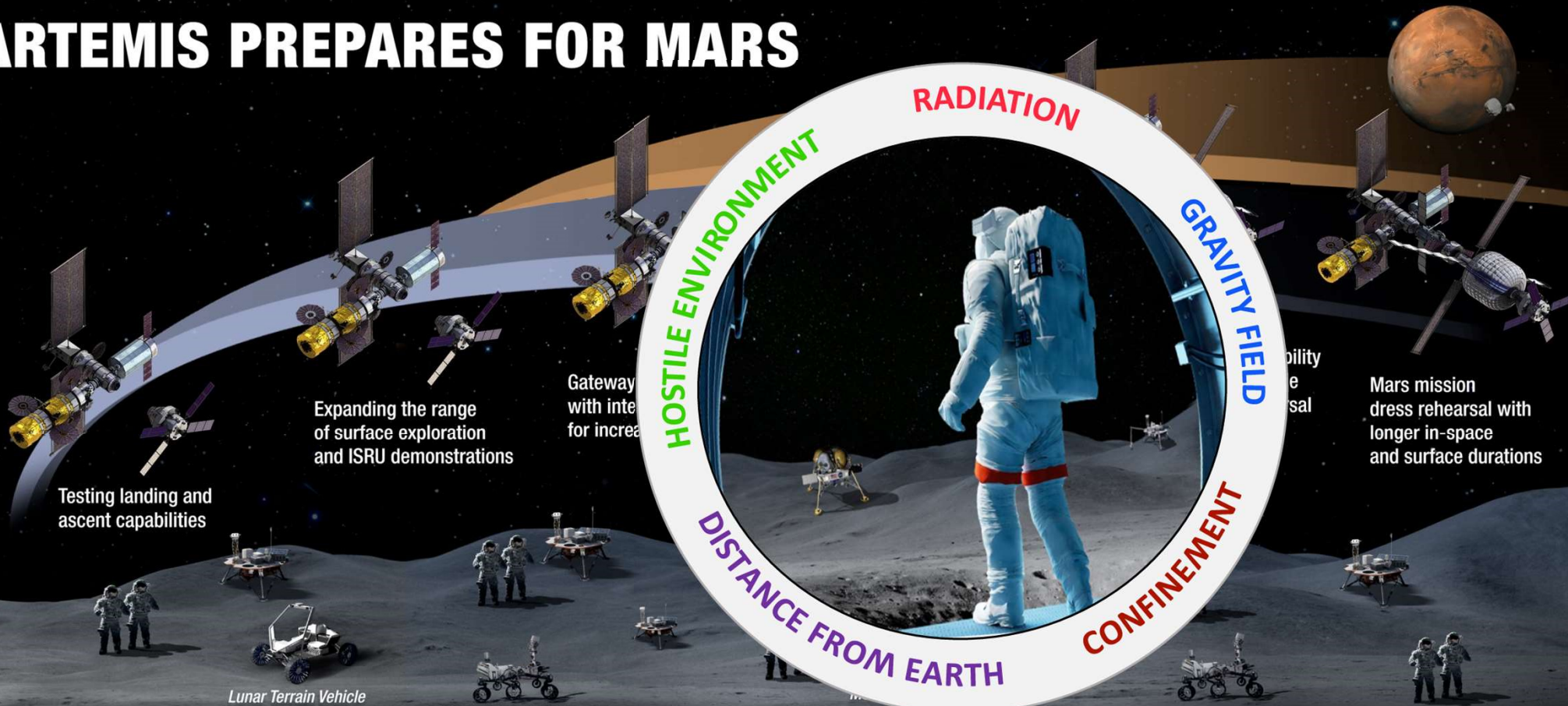
Genomic and Phenotypic Associations to Predict Human Sensitivity to Space Radiation

Biological and
Physical Sciences

Sylvain Costes
NASA Ames Research Center



ARTEMIS PREPARES FOR MARS



SUSTAINABLE LUNAR ORBIT STAGING CAPABILITY AND SURFACE EXPLORATION

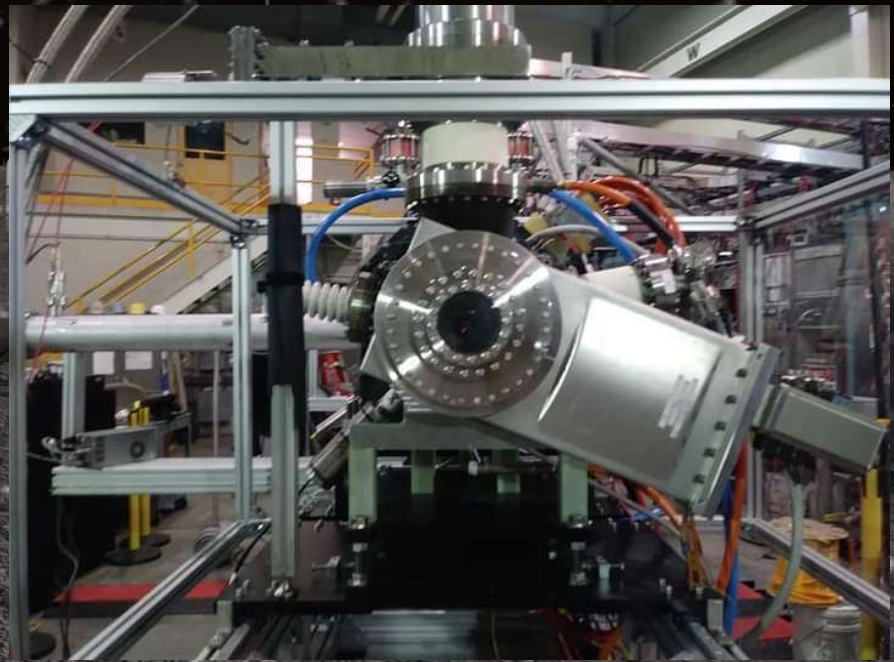
MULTIPLE SCIENCE AND CARGO PAYLOADS | INTERNATIONAL PARTNERSHIP OPPORTUNITIES | TECHNOLOGY AND OPERATIONS DEMONSTRATIONS FOR MARS

Galactic Cosmic Rays:

~87% protons

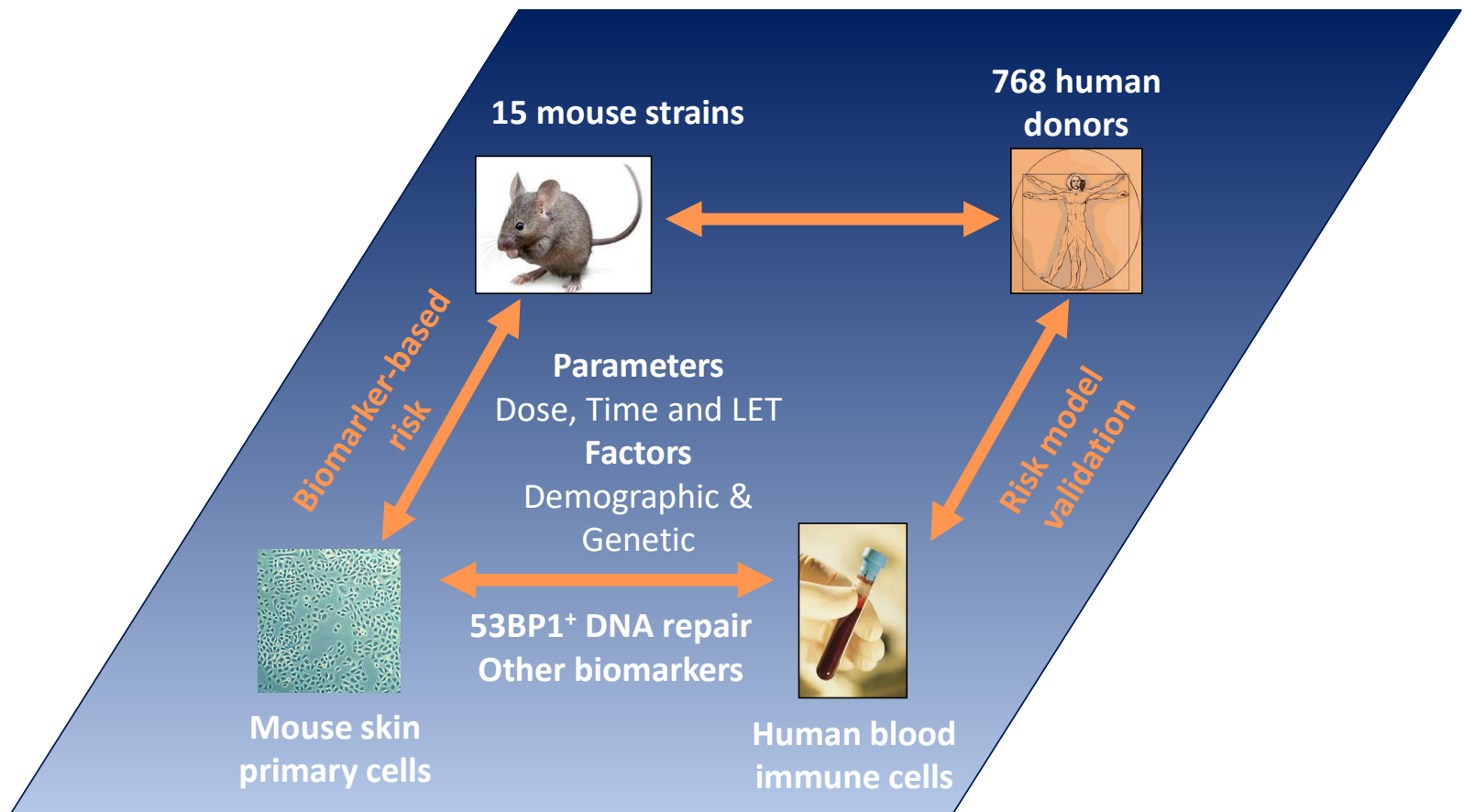
~12% ^4He

~1% high mass-charge particles through ^{56}Fe

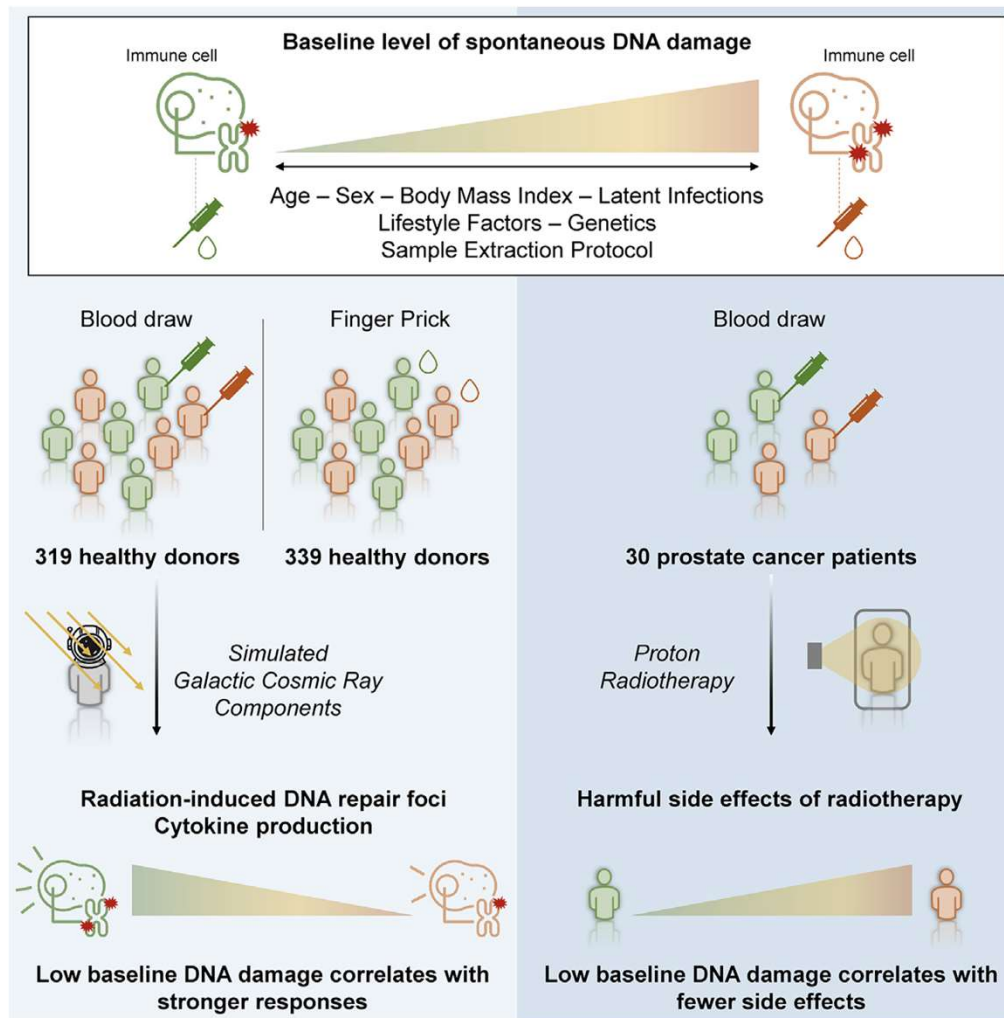


Simulated at NASA Space Radiation Laboratory in Brookhaven National Lab

Blood-based multi-scale model for cancer risk from GCR in genetically diverse populations

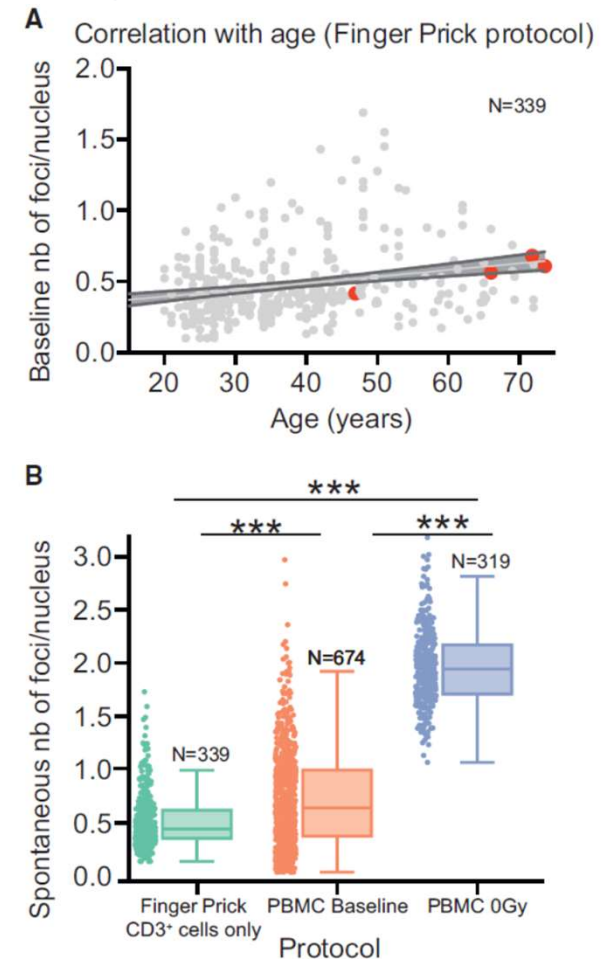
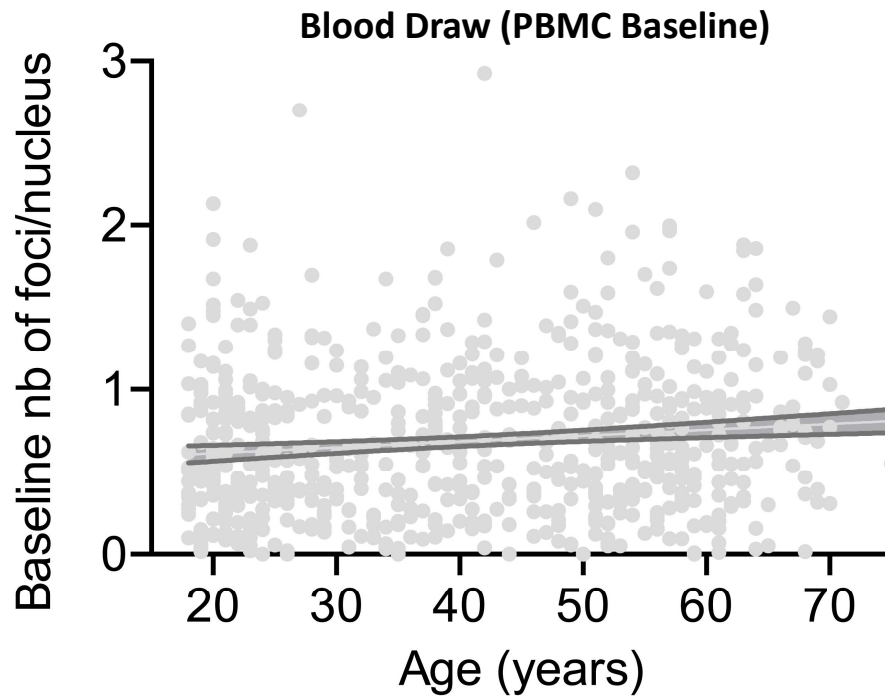
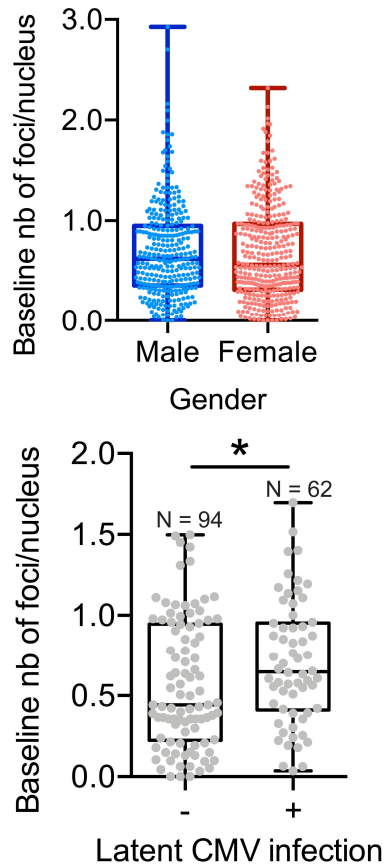


Baseline DNA damage predicts radiosensitivity

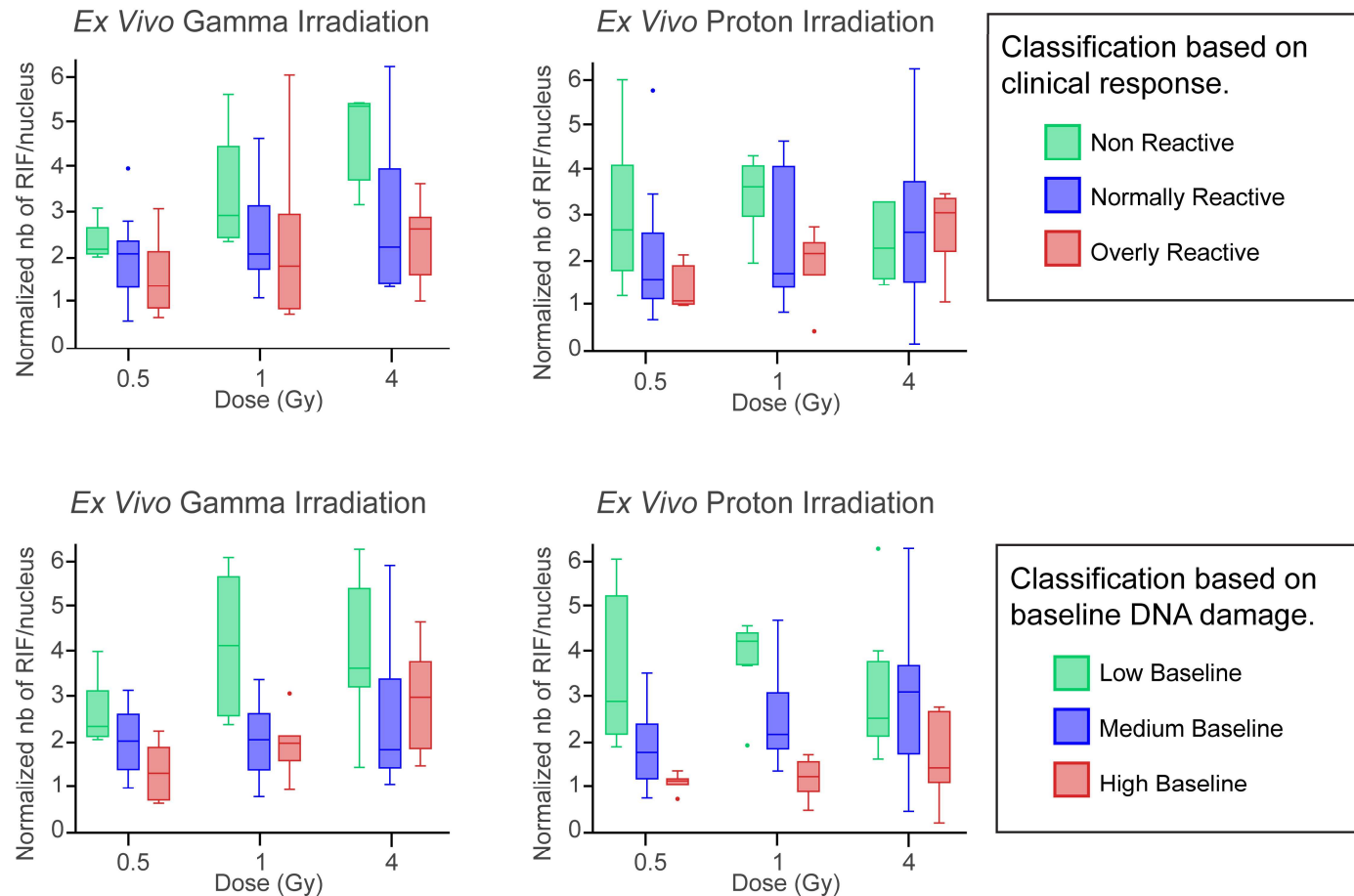


Pariset et al., Cell Reports 2020

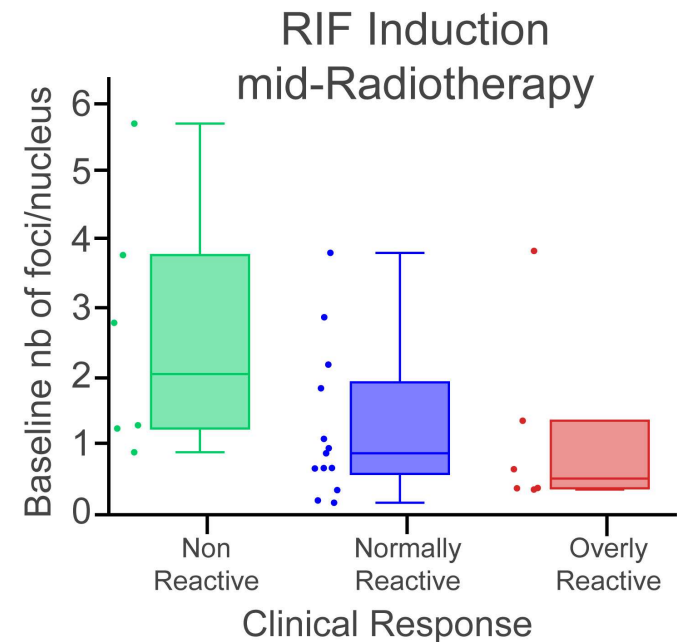
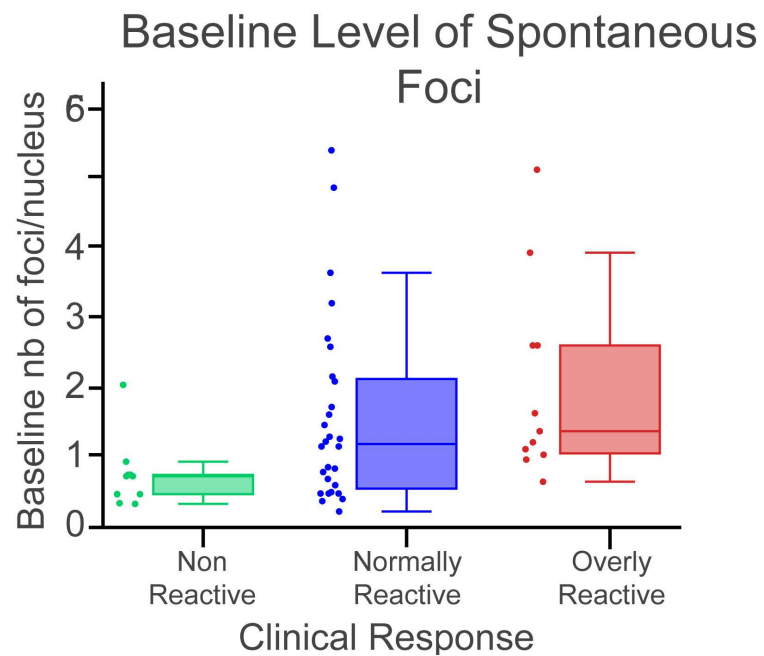
Baseline DNA damage increases with age and CMV infection



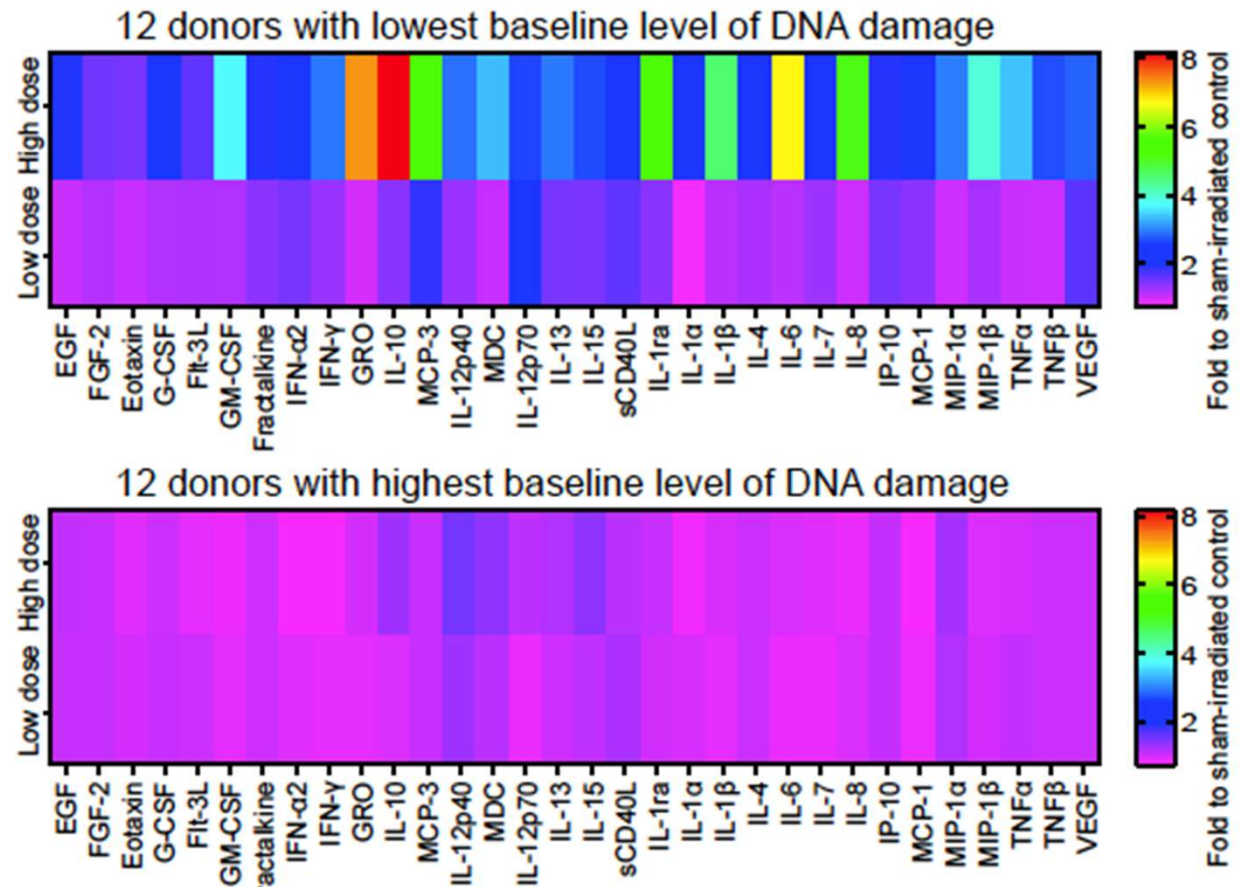
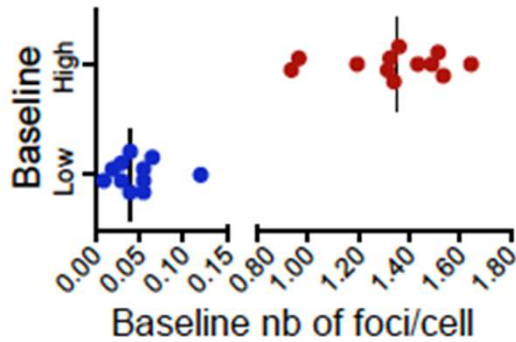
Baseline DNA damage predicts radiosensitivity in patients *ex vivo*



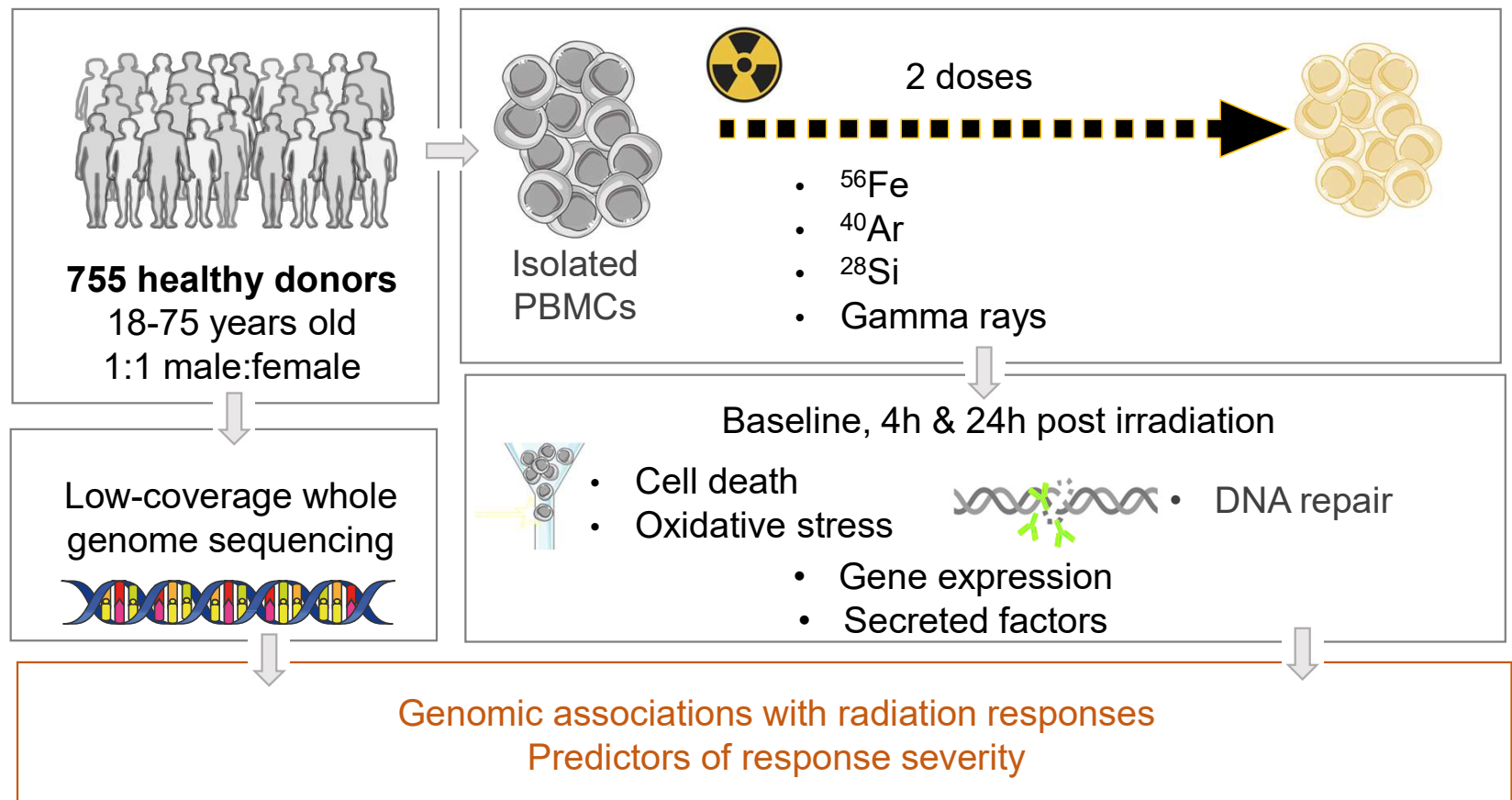
Baseline DNA damage predicts radiosensitivity in patients *in vivo*



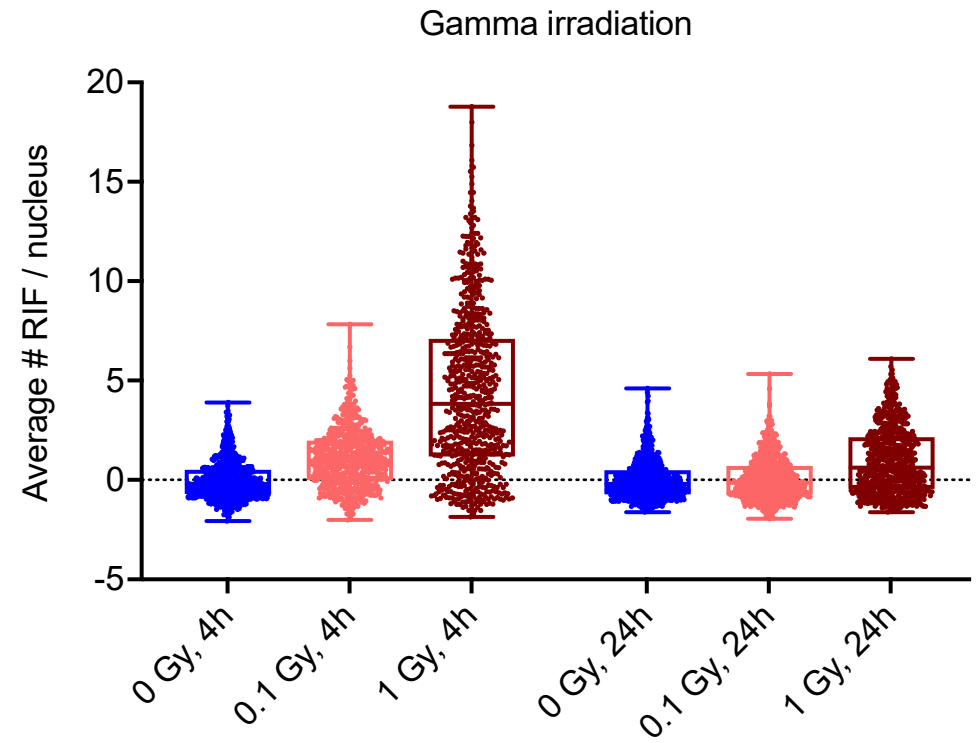
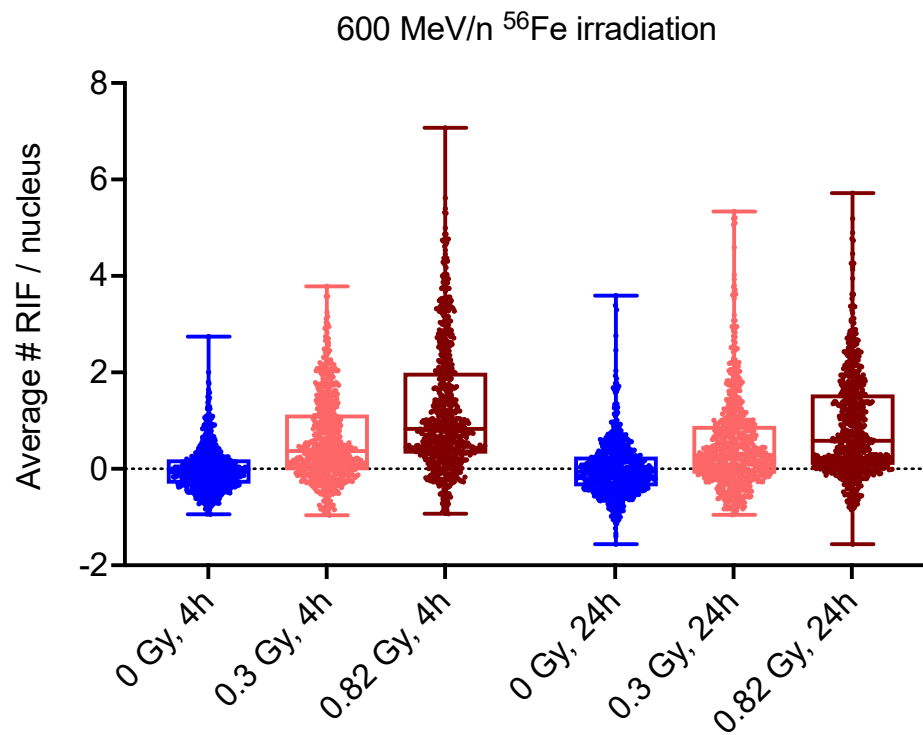
Baseline DNA damage predicts radiosensitivity in healthy donors *ex vivo*



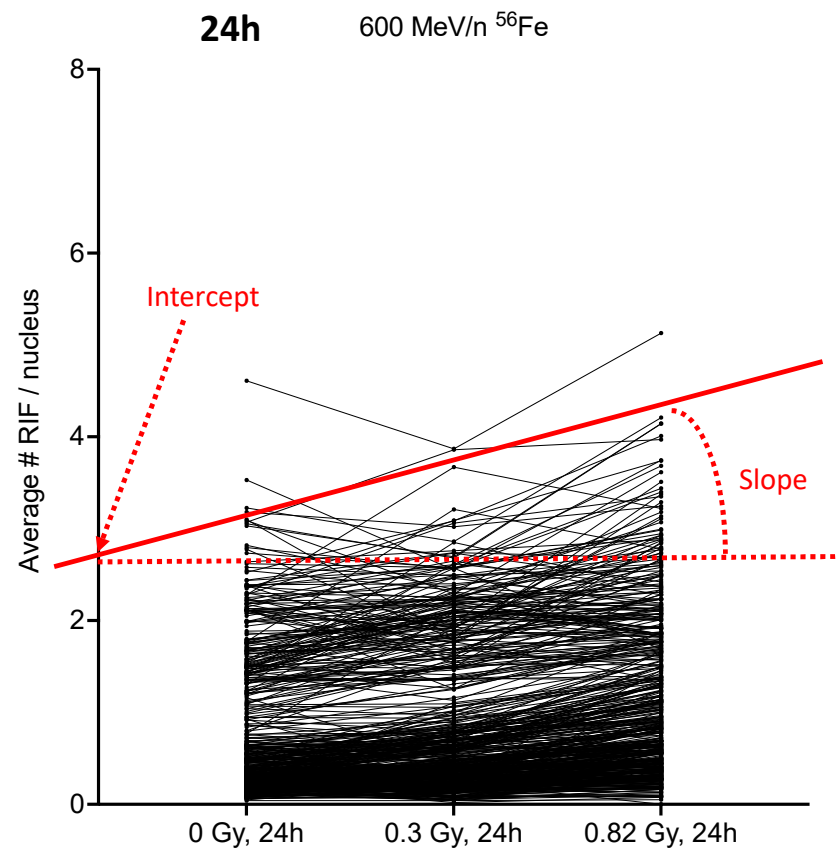
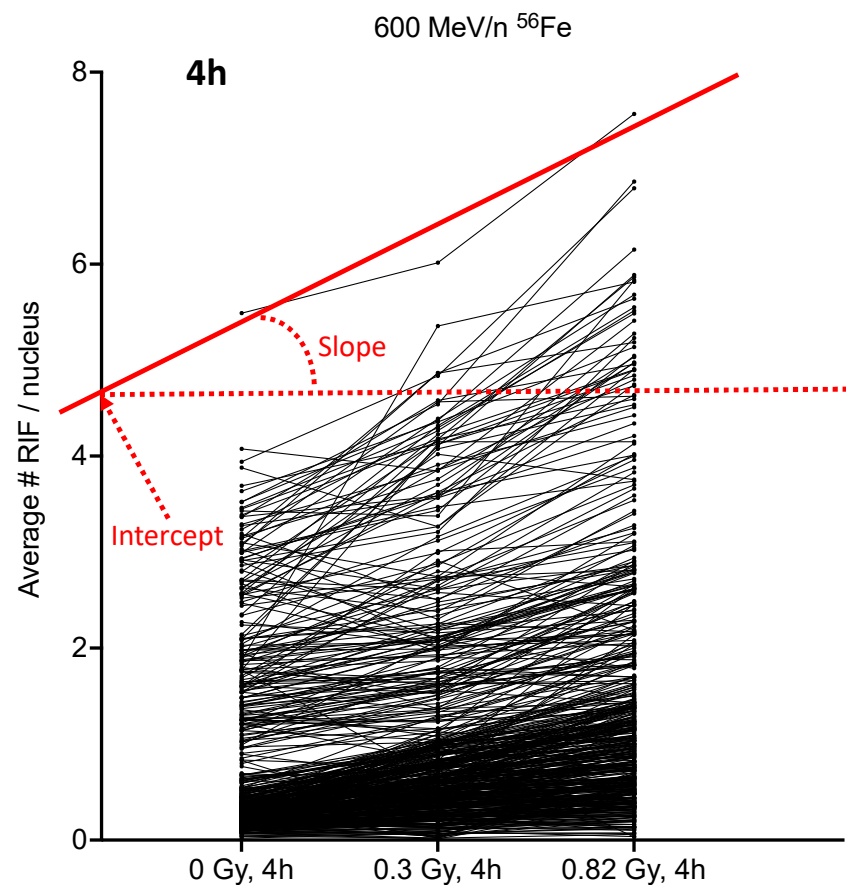
Experimental setup



Radiation-induced DNA damage



Defining radiosensitivity: slopes to describe the *rate* of radiation-induced DNA damage

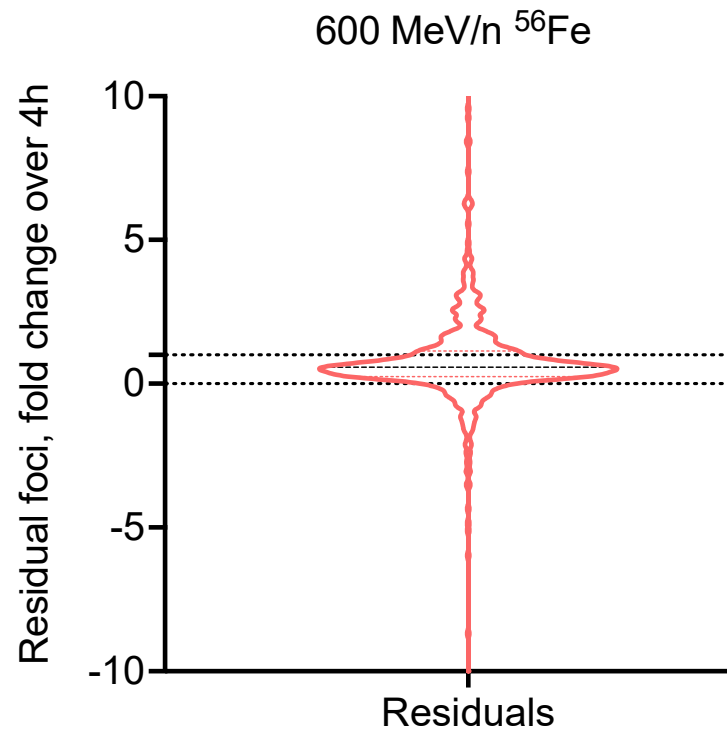


Defining radiosensitivity: residual foci at 24h to describe *persistent* radiation-induced DNA damage

$$(\text{IR, 24h} - \text{Sham, 24h}) / (\text{IR, 4h} - \text{Sham, 4h})$$

IR: high dose of irradiation (0.82 Gy for Fe)

Sham: 0 Gy irradiation control



Radiosensitivity score to describe the response *pattern*

FPG = Foci Per Gray

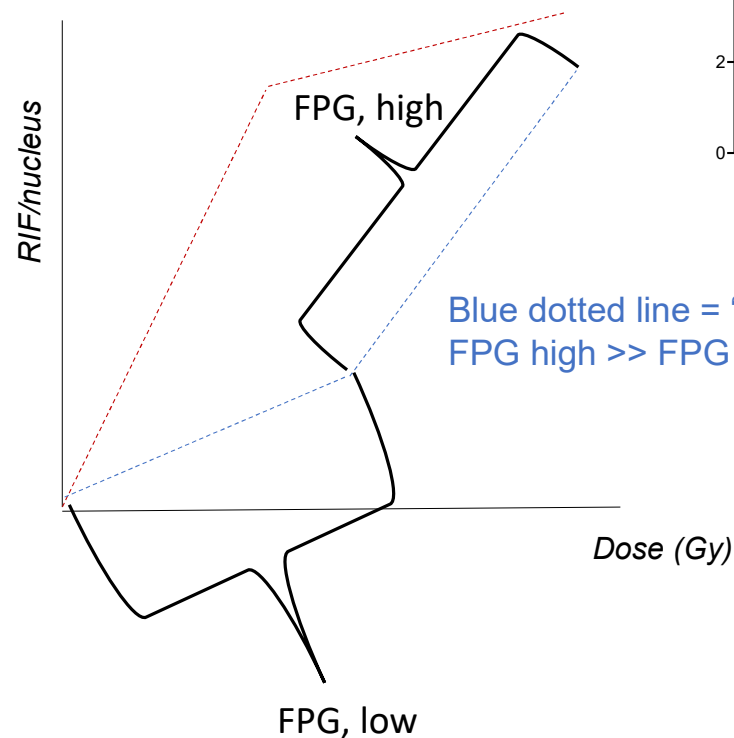
- $\text{FPG high} = (\text{RIF, 0.82 Gy} - \text{RIF, 0.3 Gy}) / (0.82 - 0.3)$
- $\text{FPG low} = (\text{RIF, 0.3 Gy} - \text{RIF, 0 Gy}) / 0.3$

$$X_i = \text{FPG high}_i - \text{FPG low}_i$$

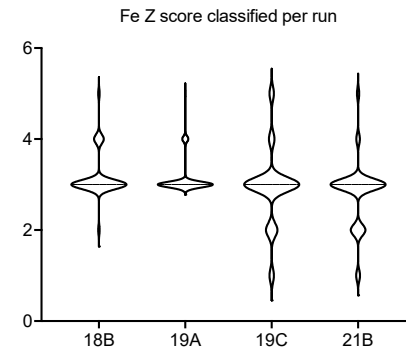
Then, scores based on mean and standard deviation:

- $X < (\text{mean} - 2\text{SD})$: score **1**
- $(\text{mean} - 2\text{SD}) < X < (\text{mean} - 1\text{SD})$: score **2**
- $(\text{mean} - 1\text{SD}) < X < (\text{mean} + 1\text{SD})$: score **3**
- $(\text{mean} + 1\text{SD}) < X < (\text{mean} + 2\text{SD})$: score **4**
- $X > (\text{mean} + 2\text{SD})$: score **5**

Red dotted line = “hypersensitive”
FPG high \ll FPG low, **score 1**

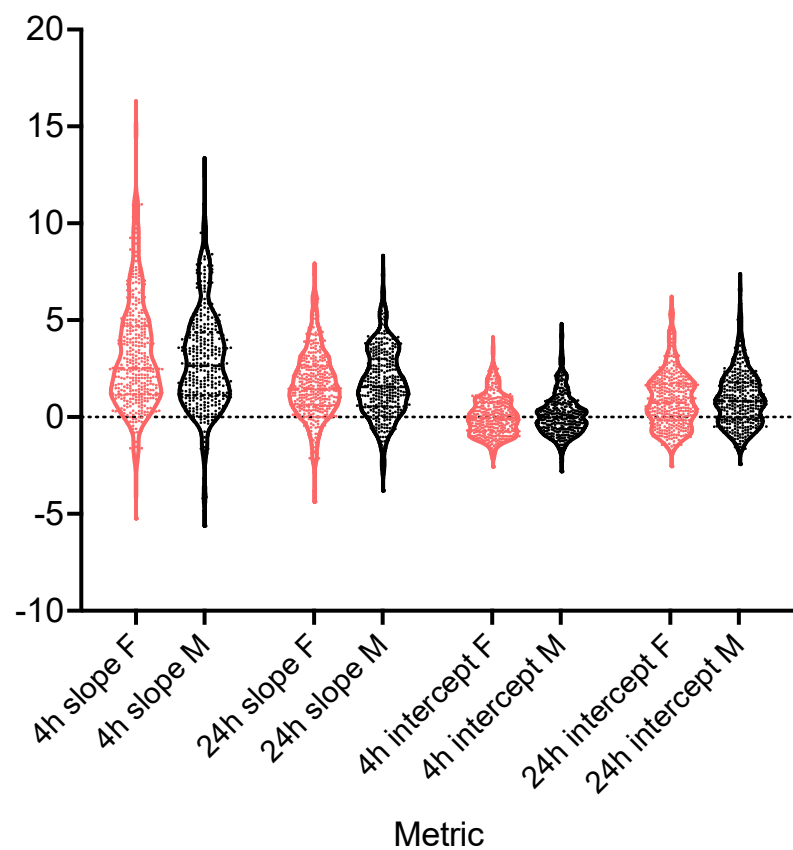


Blue dotted line = “hyposensitive”
FPG high \gg FPG low, **score 5**

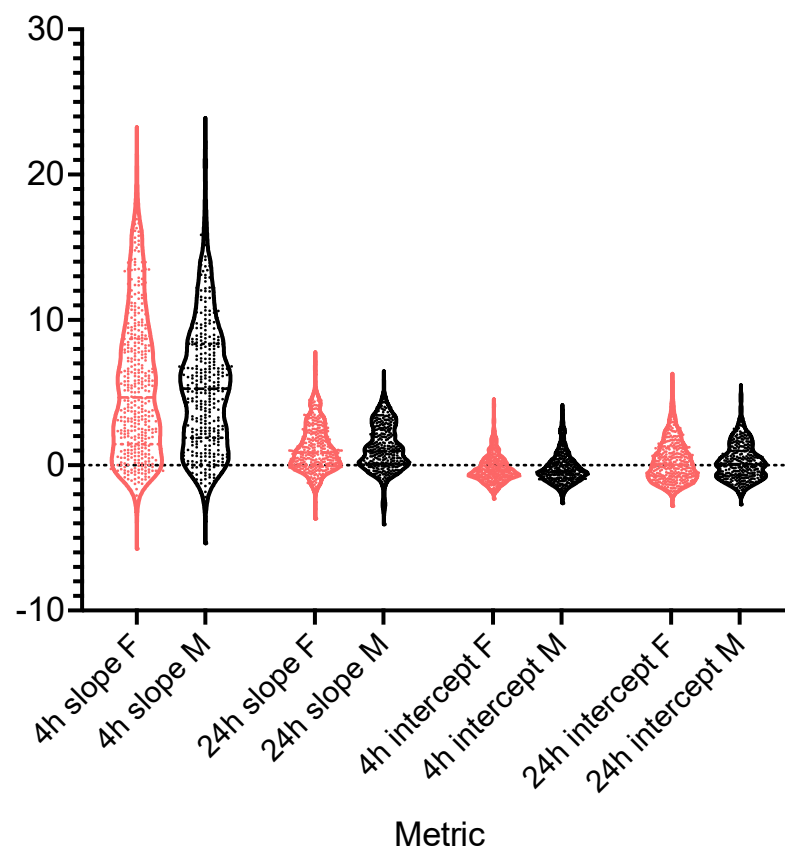


No sex differences in DNA repair responses

600 MeV/n ^{56}Fe : Slopes and Intercepts by Sex

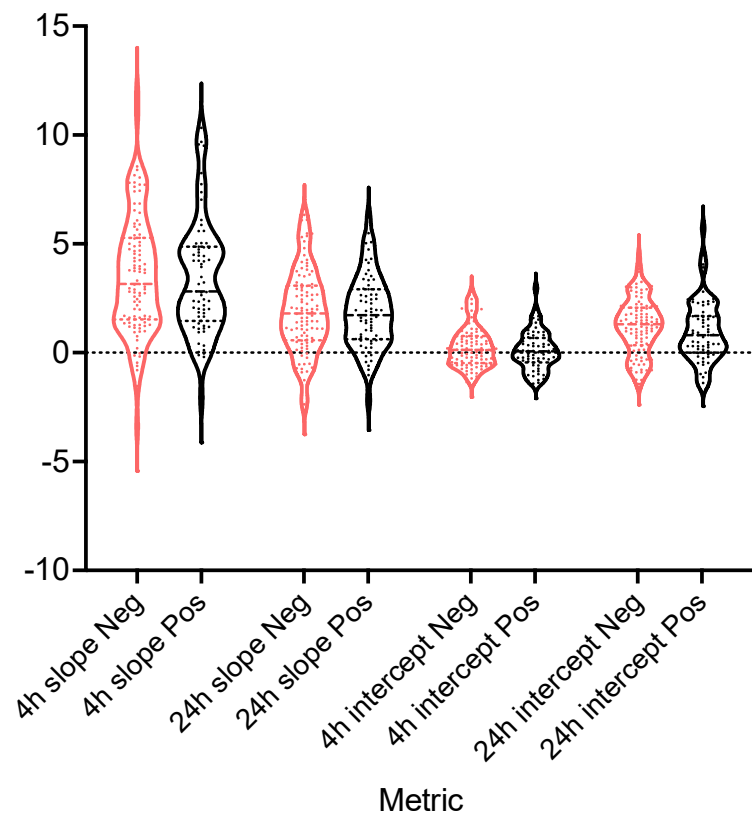


Gamma: Slopes and Intercepts by Sex

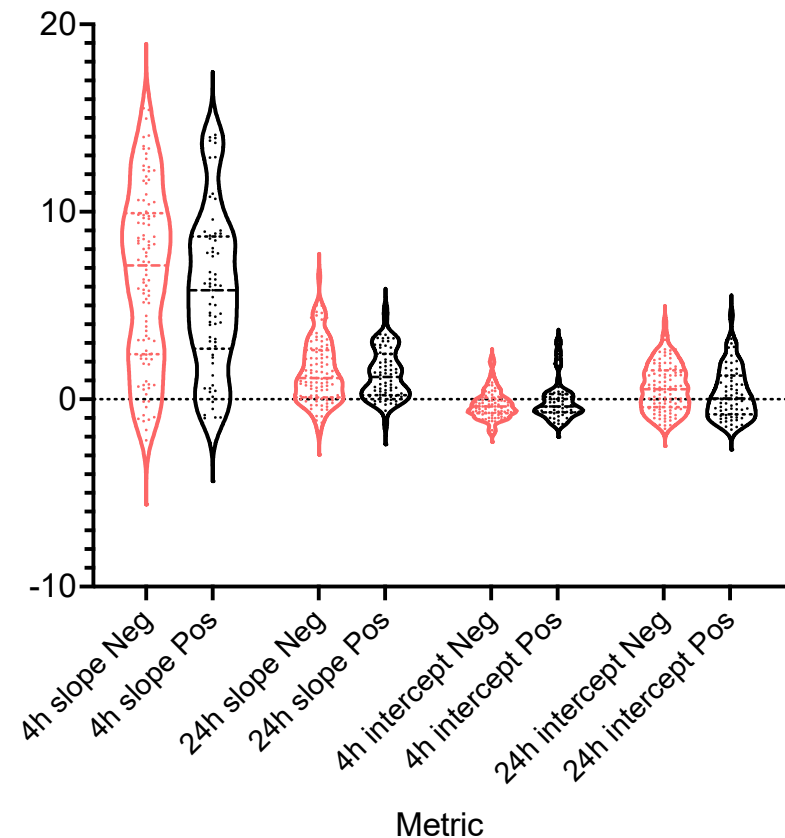


No differences in DNA repair responses based on CMV status

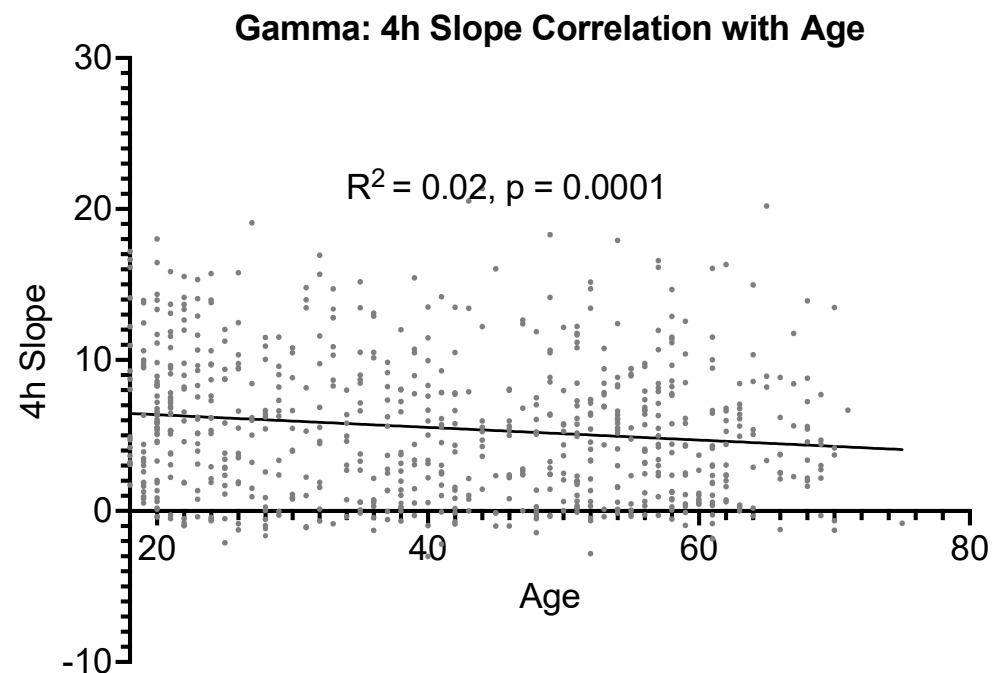
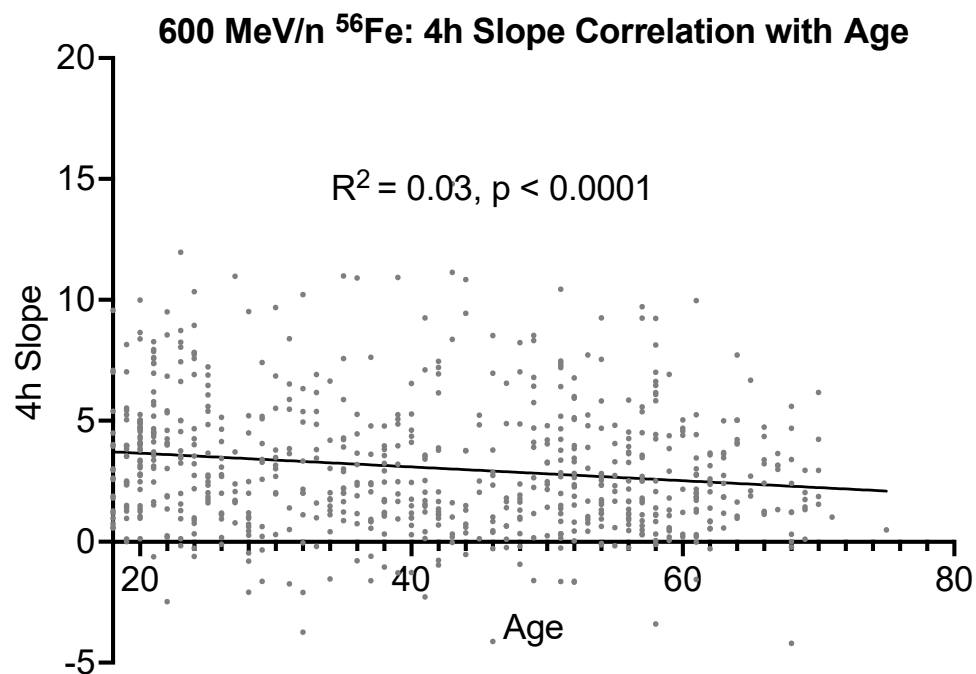
600 MeV/n ^{56}Fe : Slopes and Intercepts by CMV Status



Gamma: Slopes and Intercepts by CMV Status

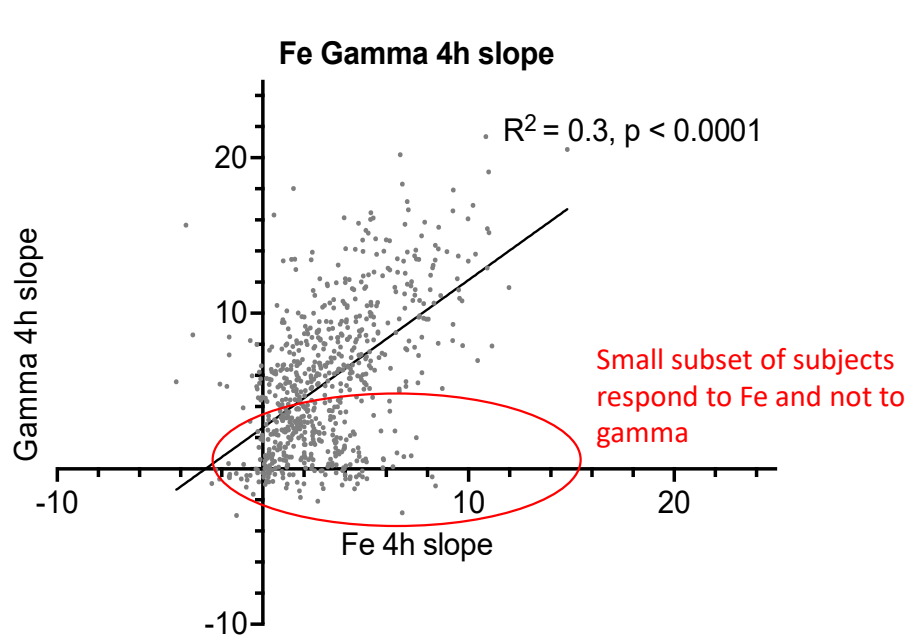


DNA repair is reduced with age

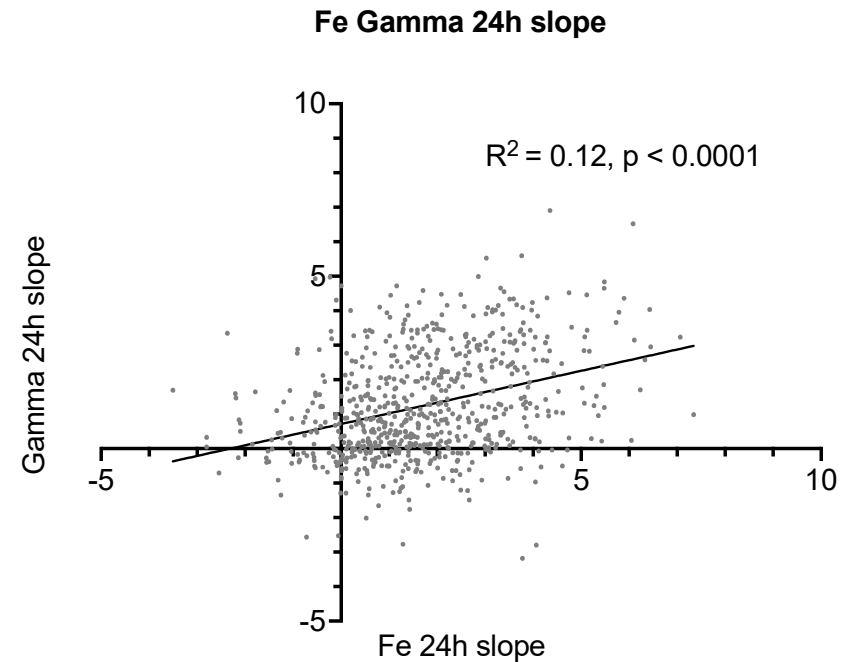


Slopes are reduced and baselines are increased with age
“Unhealthy” response: high baseline, low repair after stressor

Comparison between DNA repair responses to 600 MeV/n ^{56}Fe particles and gamma rays

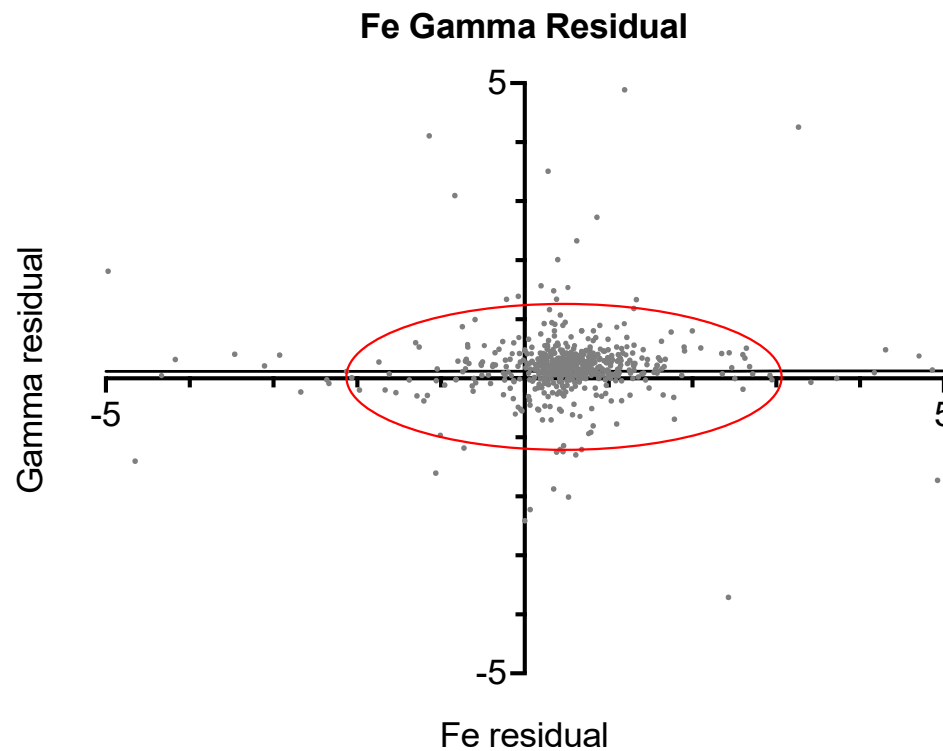


Steeper in gamma than in Fe: Fe leads to clustering of repair sites



Steeper in Fe than in gamma: remaining damage

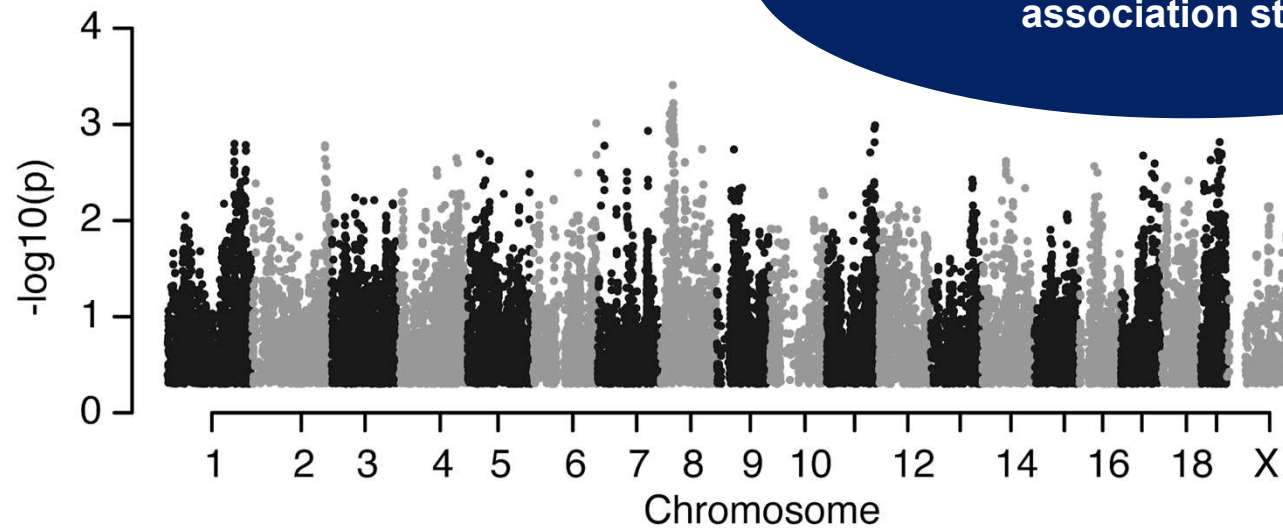
Comparison of residual DNA damage caused by 600 MeV/n ^{56}Fe particles and gamma rays

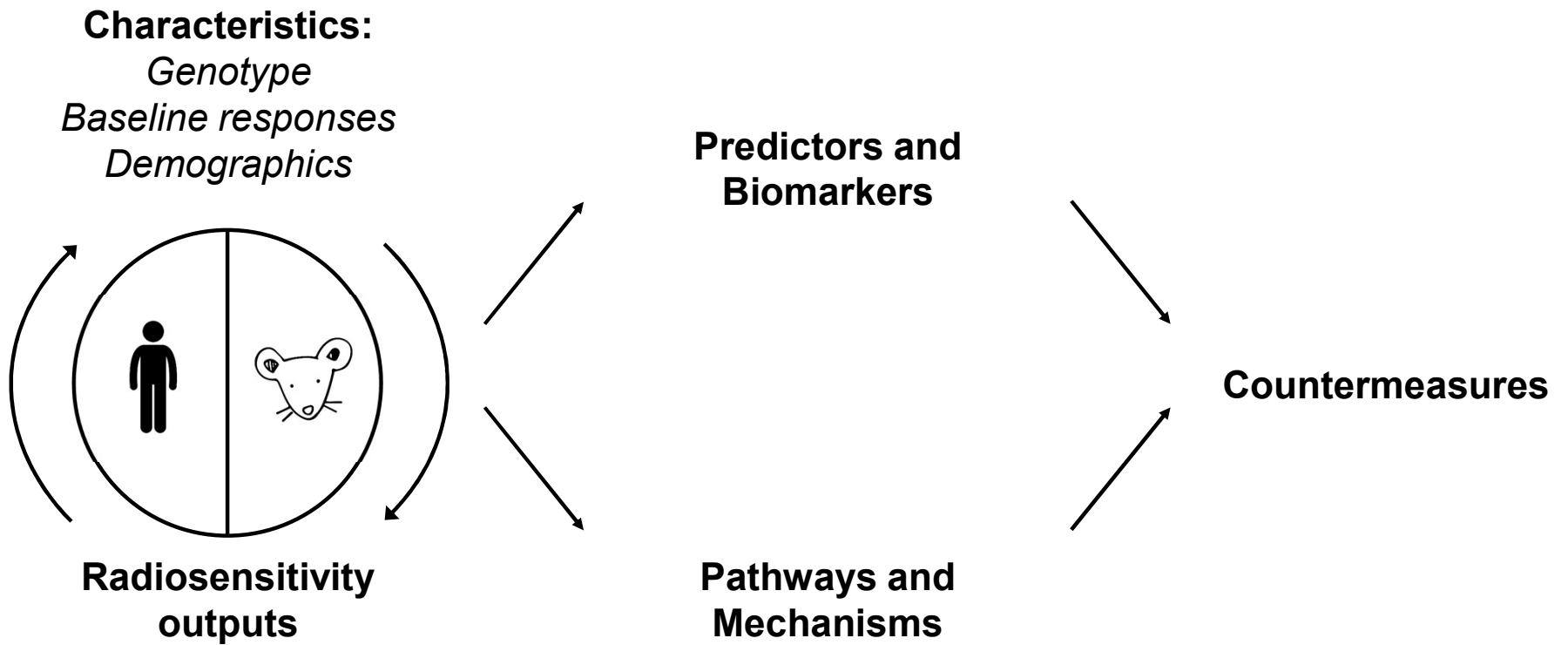


More in Fe than in gamma and not correlated (Fe, not gamma leads to prolonged response)

Genomic associations with radiosensitivity: ongoing!

Representative image from the
associated *mouse* genomic
association study





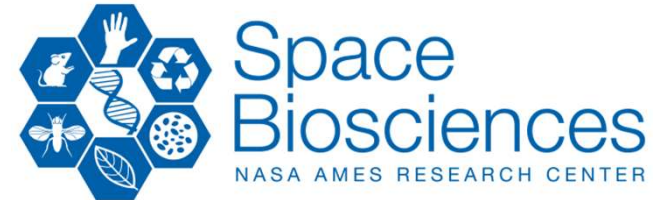
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